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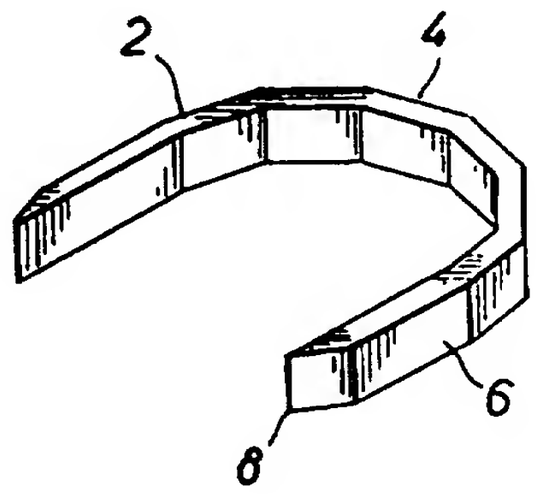
(57) Abstract

The present invention provides a shape-memory hemostatic staple (2). An article of manufacture comprising a shape-memory nickel-titanium alloy staple, said staple composed of 100 % shape-memory nickel-titanium alloy. Also provided is method of inducing hemostasis in a bleeding vessel, comprising the steps of: contacting said vessel with a shape-memory hemostatic staple; and applying heat to said staple so that said staple deforms leading to hemostatis in said vessel.



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SHAPE-MEMORY HEMOSTATIC STAPLE

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates generally to the fields of medical devices and biomedical engineering. More specifically, the present invention relates to a shape-memory hemostatic staple.

Description of the Related Art

Upper gastrointestinal bleeding is a common phenomenon accounting for 10% of acute hospital admissions in the United States. Upper gastrointestinal hemorrhage represents a clinical state caused of a variety of etiologies with varying incidence depending, at least in part, on hospital demographics. Possible etiologies for upper gastrointestinal hemorrhage include hemorrhage from gastric and duodenal ulcers, erosive gastritis, Mallory-Weiss tears, esophagitis, marginal ulcerations, bleeding tumors, duodenitis and angiodysplasia. The remaining cases are due to bleeding esophageal or gastric varices.

Most studies indicate about a 50% incidence of upper gastrointestinal bleeding secondary to peptic ulcers, with duodenal ulcers more common than gastric ulcers. Approximately 75% to 85% of hemorrhages will subside spontaneously and require no intervention other than diagnostic endoscopy. Conditions such as erosive gastritis, esophagitis and duodenitis are treated by medical

means alone, i.e., without surgical intervention. Mallory-Weiss tears stop bleeding spontaneously in a high percentage of cases. Because of the high mortality associated with persistent bleeding, efforts have centered upon the identification of patients at great risk for continued or recurrent bleeding.

Consensus is currently being reached as to which clinical manifestations are most likely to subsequently require endoscopic intervention. Recent interest has focused on such clinical features as hematemesis, hypotension or bright red blood exuded from the rectum. Endoscopically, the findings of active spurting or oozing, a visible vessel within an ulceration or a "sentinel clot", clearly indicate the need for intervention. The most common diagnosis associated with high risk bleeding is peptic ulcer disease. Approximately 100,000 such cases are treated in the United States yearly.

Therapeutic endoscopy has made great advances since the first report of successful endoscopic therapy for gastrointestinal bleeding published by Crafoord and Frenckner in 1939. Crafoord and Frenckner used rigid esophagoscopy and variceal injection of a quine-urethane solution to treat a patient with variceal hemorrhage. Modern endoscopic therapeutic approaches include 5 principle methods for hemostasis: (1) injection of sclerosing agents, (2) contact thermo-coagulation techniques which include monopolar or bipolar electrocautery and heater probes, (3) laser, (4) topical hemostatic agents and (5) injected vasoconstrictors.

The three primary endoscopic treatments are bipolar coagulation, heater probe and injection therapy. The overall efficacy of these modalities is excellent with successful hemostasis reported in 70%-95% of cases, depending on technique, number of applications and the type of bleeding. Bleeding from visible vessels is a common

problem. Traditional endoscopic treatment is successfully carried out in 30% - 50% of these patients. The motility of rebleeding is 18%-30%.

The main cause of death in gastrointestinal bleeding is not exsanguination but cardiovascular complications, hepatic and renal failure and septic complications. Therefore, many centers consider immediate operation in these patients. Prior to effective endoscopic techniques for hemostasis, it was estimated that 10-20% of upper gastrointestinal bleeders would ultimately require surgery.

Complications of traditional endoscopic treatment are relatively rare. The most important being perforation which occurs with an incidence of <1%. Other complications include reactions to medications, aspiration, arrhythmias and hemorrhage related to instrumentation and infections.

Endo-organ surgery represents a hybrid approach between diagnostic upper gastrointestinal endoscopy and therapeutic laparoscopy and PEG placement and poses numerous potential risks. Traditionally, esophago-gastroduodenoscopy (EGD) has had attendant risks of aspiration, reactions to sedative medications, cardiac arrhythmias, bleeding related to instrumentation and a risk of perforation. Since perforation secondary to traditional endoscopic therapy carries an approximate 16% mortality rate, close monitoring is required. This problem may, however, be managed quite satisfactorily by endo-organ suturing techniques should it occur in this setting. The risks of endo-organ surgery are related to possible bowel injury incurred during introduction of operative ports. These risks of endo-organ surgery should be minimized by following standardized techniques employed during percutaneous endoscopic gastrostomy.

Overall mortality for patients with bleeding ulcers has remained relatively stable. This is due to the fact that most fatalities are caused by bleeding ulcers with visible vessels in their base and these types of bleeding ulcers show a poor response to endoscopic therapy. However, the prior art remains deficient in the lack of effective means of treating bleeding ulcers and other types of gastrointestinal hemorrhagic conditions. The present invention fulfills this longstanding need and desire in the art.

SUMMARY OF THE INVENTION

In one embodiment of the present invention, there is provided an article of manufacture comprising a shape-memory hemostatic staple.

In another embodiment of the present invention, there is provided an article of manufacture comprising a shape-memory nickel-titanium alloy staple, said staple composed of approximately 100% shape-memory nickel-titanium alloy.

In still yet another embodiment of the present invention, there is provided a method of inducing hemostasis in a bleeding vessel, comprising the steps of: contacting said vessel with a shape-memory hemostatic staple; and applying heat to said staple so that said staple deforms leading to hemostasis in said vessel.

Other and further aspects, features, and advantages of the present invention will be apparent from the following description of the presently preferred embodiments of the invention given for the purpose of disclosure.

BRIEF DESCRIPTION OF THE DRAWINGS

So that the matter in which the above-recited features, advantages and objects of the invention, as well as others which will become clear, are attained and can be understood in detail, more particular descriptions of the invention briefly summarized above may be had by reference to certain embodiments thereof which are illustrated in the appended drawings. These drawings form a part of the specification. It is to be noted, however, that the appended drawings illustrate preferred embodiments of the invention and therefore are not to be considered limiting in their scope.

Figure 1 shows a schematic diagram of a duodenal ulcer with suturing for hemostasis.

Figure 2 shows a side elevated view of one embodiment of the staple of the present invention in the unformed shape.

Figure 3 shows a side view of one embodiment of the staple of the present invention in the unformed shape.

Figure 4 shows a top view of a flattened unformed staple of the present invention.

Figure 5 shows a side view of one embodiment of the staple of the present invention in the formed shape.

Figure 6 shows the temperature range during which transformation of the shape-memory nickel-titanium alloy staple of the present invention takes place. A_S is the temperature at the start of austenitic transformation while heating. A_f is the temperature at which austenitic transformation is complete. M_S is the temperature at the start of martensitic transformation while cooling. Mf is the

temperature at which martensitic transformation is complete. T is the body temperature.

Figure 7 shows a schematic diagram of the staple sharpness test.

Figure 8 shows a schematic diagram of the maximum pressure test.

Figure 9 shows a schematic diagram of the formation pressure test.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides a hemostatic staple made from a shape-memory nickel-titanium alloy known as NITINOL™. One use of the shape-memory hemostatic staple of the present invention is introduction around an actively bleeding ulcer. The staple can be introduced scopically through the Cook Surgical GI Access Tube directly to the pyloric region by means of a thin applicator. A person having ordinary skill in this art would recognize that an entirely endoscopic procedure may also be performed. Rather than mechanically deforming the staple to compress the tissue and affect hemostasis, a small amount of electrical current is passed through the staple or, alternatively, heat is directly applied to the staple. Electrical resistance/direct heat will cause the staple to heat to about 45 to 60 degrees Celsius and the staple will quickly and forcibly deform itself to the desired configuration i.e., reform to its memory shape. It is contemplated that a titanium shell around the shape-memory nickel-titanium alloy is useful in maintaining the desired pressure after the staple formation is complete. A person having ordinary skill in the art of biomedical engineering would

readily recognize the methodology required to place such a titanium shell around the shape-memory hemostatic staple of the present invention.

The shape-memory nickel-titanium alloy staple is designed so as to impart sufficient tissue compression to affect hemostasis of an actively bleeding peptic ulcer. The staple of the present invention is applied and formed in an easy and safe manner.

The staple, when heated sufficiently for shape recovery (shape change), does not unduly damage the surrounding tissue. That is, any burning of the surrounding tissue is minimal and inconsequential. For example, a standard therapeutic endoscopy heater probe cauterizes tissue at up to an estimated 600° C. It is also specifically contemplated that the staple can be thermally insulated without reducing sharpness and effectiveness. For example, one may apply a thin polymeric coating to the staple and thereby decrease the amount of heat being transferred to the surrounding tissues.

The present invention shows that endo-organ surgery using a shape-memory nickel-titanium alloy staple is an effective method for establishing hemostasis and thus hopefully improves the survival of patients with upper gastrointestinal bleeding. In addition, application of a similar staple via endoscopic means alone has other valuable applications.

The present invention is directed to an article of manufacture comprising a shape-memory hemostatic staple. Generally, the shape-memory staple of the present invention has a compression ratio which allows said staple to deform subsequent to application of heat so that the formed staple has a shape-memory hemostatic effect on the blood vessel, or even surrounding tissues, it engages. Preferably, the staple has a minimal tissue compression

ratio of approximately 3.8. A higher tissue compression ration is possible provided the tissue does not become more resistant.

The shape-memory staple of the present invention has other desirable characteristics. For example, the staple preferably has a temperature at the start of austenitic transformation while heating of from about 30°C to about 45°C. Also, the staple preferably has a temperature at the start of martensitic transformation while cooling of from about 60°C to about 40°C.

In a preferred embodiment of the present invention, the staple is composed of shape-memory nickel-titanium alloy. Generally, the percentage of shape-memory nickel-titanium alloy is that amount of shape-memory nickel-titanium alloy which conveys the characteristics to the staple of the present invention. Preferably, the staple is composed of approximately 100% shape-memory nickel-titanium alloy.

In another preferred embodiment of the present invention, the staple is a composed of shape-memory nickel-titanium alloy and bears a titanium sheath over the staple.

It is specifically contemplated that the staple of the present invention may be thermally insulated. Thermal insulation may be desirable if a pre-cooled staple is used or if the formation temperatures are excessively high.

It is generally considered that the shape-memory hemostatic staple described herein is deformed *in situ* by application of heat. Although there are various ways of applying heat to the staple, a preferred method is by an electrical current. Heat can be electrically applied to the staple in two ways. One application of heat to the staple is via simple monopolar current passed from the application grasper (cathode), through the staple and out through the

grounding pad onto, e.g., the patient's thigh. Monopolar cautery current may be used provided one does not use an amperage which transfers excessive heat to surrounding tissue. A second application of heat to the staple comprises manufacturing the staple so that the tip of each staple leg has a small thin wire for contact. Current passing through the staple will then affect the shape transformation. Alternatively, the staple may be deformed by application of direct heat. For example, a heater can be placed in the applicator with which the staple and surrounding tissue would be heated to the transformation temperature. Another method is to set the staple to have its own transformation temperature below body temperature. The staple would be applied under a cold saline bath and the body temperature would affect the shape transformation. However, this latter method is least preferred.

The present invention is also directed to a shape-memory nickel-titanium alloy staple, said staple composed of approximately 100% shape-memory nickel-titanium alloy. In addition, this shape-memory nickel-titanium alloy staple may further comprise a titanium sheath covers said staple. The shape-memory nickel-titanium alloy staple of the present invention preferably has a tissue compression ratio of from about 3.8 to about 4.0. The shape-memory nickel-titanium alloy staple of the present invention preferably has a temperature at the start of austenitic transformation while heating of from about 30°C to about 45°C. The shape-memory nickel-titanium alloy staple of the present invention preferably has a temperature at the start of martensitic transformation while cooling of from about 60°C to about 40°C.

The present invention is also directed to a method of inducing hemostasis in a bleeding vessel, comprising the steps of:

contacting said vessel or surrounding tissue with a shape-memory hemostatic staple; and applying heat to said staple so that said staple deforms leading to hemostasis in said vessel. This method is applicable to inducing hemostasis in a wide variety of blood vessels in different clinical states. For example, the shape-memory nickel-titanium alloy staple of the present invention would be very useful in stopping a actively bleeding ulcer.

The following examples are given for the purpose of illustrating various embodiments of the invention and are not meant to limit the present invention in any fashion.

EXAMPLE 1

A special Endo-organ port (GI Access Tube) has been developed which allows percutaneous access to the gastric lumen. The technique of port placement into the stomach by a procedure similar to percutaneous endoscopic gastrostomy (PEG) has proven successful. In fourty-two prototype gastric access ports that were placed, only three had malfunctions.

An upper endoscopy was performed to distend the gastric cavity by air insufflation and to trans-illuminate through the anterior abdominal wall. A needle was introduced through the transilluminated wall into the stomach. A loop-guidewire was advanced into the gastric cavity, snared by biopsy forceps passed through the scope and pulled out transorally. A dilator assembly with the port at the proximal end was introduced over the taught guidewire into the stomach and pushed through the abdominal wall. A second port was placed by the same technique. Through one port, the laparoscope was introduced; the other port was used to advance

the stapler or needle holder into the gastric cavity. This approach provides good visualization of the entire stomach and efficient use of stapling or suturing instruments was possible within the gastric cavity. Suturing within the first portion of the duodenum after pyloric dilitation has proven difficult. Assuming that the four-quadrant suture ligation of the posterior bleeding ulcer was the standard-of-care and was to be duplicated by the endo-organ approach, laboratory efforts have been unsuccessful. Because the duodenum is a confined space, the needle for suturing large, deep sutures oriented caudad and cephalad of the ulcer base cannot be applied. This was established after seven experimental operations. The distal and proximal sutures (Figure 1) can be placed but not deeply. In *ex vivo* studies and on ultrasonic examination of sutures placed in the human to ligate a bleeding duodenal ulcer, the tied suture is 8 mm deep. In the present invention, a new device was designed to duplicate the depth of penetration, tissue compression and shape of the traditional ligating suture.

EXAMPLE 2

Staple Design

According to the prior art, a large staple having the dimensions of 10 mm wide, 2 mm thick with a leg length of 10 mm would sufficiently penetrate tissue. Preferably, the staple compresses tissue to the same degree as a deep suture. For suturing, a compression ratio of 3.8 is desirable to maintain an adequate ligation. The compression ratio is the ratio of the enclosed cross-sectional area of an unformed staple to that of the enclosed cross-sectional area of a

formed staple. To achieve this compression, the shape-memory nickel-titanium alloy staple of the present invention must curl back upon itself to reduce its cross-sectional area sufficiently. To do this, the unformed staple will look like Figure 2 but will revert to its memory shape of an estimated 6 mm diameter coil (Figure 3) or a similar geometry with the same compression ratio.

Figure 2 shows a side elevated view of the unformed staple of the present invention. In this embodiment of the present invention, the staple 2 is composed of a crown 4 having a leg member 6. The leg 6 has a pointed end 8 to allow the staple to penetrate and grasp tissue.

Figure 3 shows a side view of the unformed staple of the present invention. In this embodiment of the present invention, the staple 2 shows a width of approximately 0.065 mm. The lower portion 10 of leg 6 in this embodiment of the present invention has an approximate height of 0.236 mm.

Figure 4 shows a top view of a flattened unformed staple of the present invention. In this embodiment having a flattened form, the staple has an approximate length of 0.394 mm.

Figure 5 shows a side view of one embodiment of the staple 2 of the present invention in the formed shape. In this embodiment, the inner diameter is approximately 6 mm.

A large titanium staple would need only to be permanently deformed to a box one-fourth of its original area but the mechanics of trying to design such a staple and fit the stapler through the 10.5 mm I.D. port are prohibitive. Thus, the present staple does that work and provides a simple and easy way to perform intraluminal stapling.

EXAMPLE 3

Material

NITINOL™ is an acronym for nickel titanium Naval Ordinance Laboratory, where it was discovered in 1962. Shape-memory nickel-titanium alloy undergoes a phase change called a "martensitic transformation" from the easily deformable, low temperature martensite form to a stronger, high temperature austenite form (Figure 4) with the addition of heat. The change is rapid and takes place in a very short temperature range. The transformation temperature for changing from martensite to austenite is higher than the transformation temperature for the changing from austenite to martensite. This hysteresis (temperature differential) is salient to the design of the staple of the present invention.

The material used to make the shape-memory hemostatic staple of the present invention was manufactured so that the core body temperature of 37°C ("T" on Figure 7) was within the hysteresis range. This was done so the material will still retain its stronger, austenitic properties while in place in the human body. During application, however, the staple will not undergo this shape change without heating the material to above body temperature. Thus, the material has $A_S > 40°C$ and $M_S < 32°C$. The narrower the hysteresis the better the material properties for the applications of the shape-memory hemostatic staple of the present invention. It is possible that a minimum hysteresis of 20°C may be a lower limit. Moreover, the higher the hysteresis, the greater strength of the material. The strength is similar to titanium, with the austenitic form 2.4 times stronger than that of the martensitic form.

EXAMPLE 4

Prototype

A sample of shape-memory nickel-titanium alloy was obtained which closely matched the final desired properties required for the staple of the present invention. The sample had a rectangular cross-section of 0.390 inches by 0.030 inches (9.9 mm by 0.76 mm). The transformation temperatures were A_s = 40 - 50°C and M_s < 32°C. The material was cut, sharpened and then the formed memory shape was imparted via a ceramic oven at 450°C for 5 minutes. Material cross-section was 0.394 inches by 0.119 inches (10 mm by 3 mm). The staples were then be mechanically strained and finely sharpened to the unformed shape.

EXAMPLE 5

Testing

The staples were examined both in the engineering lab and in the Surgical Research Laboratory. Mechanical testing comprises observing staple sharpness and rigidity during penetration of the muscle and connective tissue in beef and chicken samples. Ease of penetration is measured as the force required to push the staple through the tissue (Figure 8). The amount of pressure the formed staple can contain and still maintain its formed geometry (i.e. staple is not pulled apart) is determined by inflating a small balloon within the formed staple with water. Pressures is measured with a water manometer as shown in Figure 9. Forces generated during the initial shape change of the staple is measured by a measuring the

amount of deflection between the two legs of the staple (Figure 10) with a spring capable of resisting the shape change on the outside of each leg. The springs will have known *k* values and the maximum applied force is determined by the equation F = -2 *k* x, where F is the maximum of 3% to 4% permanent deformation will occur over the first several hundred cycles. Generally, the shape-memory hemostatic staple of the present invention desirably holds its shape at maximum strength for about 10 to about 14 hours.

EXAMPLE 6

Two staples are placed around a mesenteric artery of a pig after an unrelated open acute surgical procedure. Heat is applied to the staple by a hair dryer (on high heat). The staples begin their memory transformation to completely deform to the programmed shape and affect hemostasis. Several items were important.

First, the staple points must be sufficiently sharp to penetrate the mesentery (which is very resistant to puncture and quite slick). Also, parts of the staple must not be covered by tissue folds so that they are not insufficiently heated. The staple should have adequate holding pressures. Alternatively, one with ordinary skill in this art could use shape-memory nickel-titanium alloy that has a transformation temperature lower than body temperature and apply the staple in a chilled saline bath, although this adds to the difficulty of the procedure.

Alternate embodiments of the shape-memory hemostatic staple of the present invention include: increasing the cross-sectional dimensions of the staple and adding a titanium sheath that plastically

deforms with the shape-memory nickel-titanium alloy and maintains holding pressures if the shape-memory nickel-titanium alloy relaxes with the removal of heat.

Options available for the application of heat to the staple are electrical heating, direct heating, immersion in warm water and changing the material properties so the staple undergoes transformation at a temperature below body temperature.

Any patents or publications mentioned in this specification are indicative of the levels of those skilled in the art to which the invention pertains. These patents and publications are herein incorporated by reference to the same extent as if each individual publication was specifically and individually indicated to be incorporated by reference.

One skilled in the art will readily appreciate that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The present examples along with the methods, procedures, treatments, molecules, and specific compounds described herein are presently representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention. Changes therein and other uses will occur to those skilled in the art which are encompassed within the spirit of the invention as defined by the scope of the claims.

WHAT IS CLAIMED IS:

CLAIMS:

1. An article of manufacture comprising a shape-memory hemostatic staple, wherein said staple has a minimal tissue compression ratio of from about 3.8.

2. The article of manufacture of claim 1, wherein said staple is composed of shape-memory nickel-titanium alloy.

3. The article of manufacture of claim 1, wherein said staple is overlaid with a sheath of titanium.

4. The article of manufacture of claim 1, wherein said staple is thermally insulated.

5. The article of manufacture of claim 1, wherein said staple is deformed by application of heat.

6. The article of manufacture of claim 5, wherein said staple is deformed by application of heat caused by an electrical current.

7. The article of manufacture of claim 1, wherein said staple is deformed by application of direct heat.

8. An article of manufacture comprising a shape-memory nickel-titanium alloy staple, said staple composed of about 100% shape-memory nickel-titanium alloy and wherein said staple has a minimal tissue compression ratio of about 3.8.

9. The article of manufacture of claim 8, wherein said staple is overlaid with a sheath of titanium.

10. The article of manufacture of claim 8, wherein said staple is thermally insulated.

11. A method of inducing hemostasis in a bleeding vessel, comprising the steps of:

contacting said vessel with a shape-memory hemostatic staple, wherein said staple has a minimal tissue compression ratio of from about 3.8; and

applying heat to said staple so that said staple deforms leading to hemostasis in said vessel.

12. The method of claim 11, wherein said vessel is a bleeding ulcer.

13. A method of inducing hemostasis in a bleeding vessel, comprising the steps of:

contacting said vessel with the shape memory hemostatic staple of claim 8; and

applying heat to said staple so that said staple deforms leading to hemostasis in said vessel.

14. A method of inducing hemostasis in a bleeding vessel, comprising the steps of:

contacting said vessel with the shape-memory hemostatic staple of claim 9; and

applying heat to said staple so that said staple deforms leading to hemostasis of said vessel.

15. The article of manufacture of claim 1, wherein said staple begins austenitic transformation as the temperature of said staple is raised above about 30°C.

16. The article of manufacture of claim 1, wherein said staple begins austenitic transformation as the temperature of said staple is raised above about 45°C.

17. The article of manufacture of claim 1, wherein said staple begins martensitic transformation as the temperature of said staple cools to below about 10°C.

18. The article of manufacture of claim 1, wherein said staple begins martensitic transformation as the temperature of said staple cools to below about 25°C.

19. The article of manufacture of claim 1, wherein said staple undergoes austenitic transformation and therefore shape change by being placed in the body and being subjected to body heat.

FIG. 1

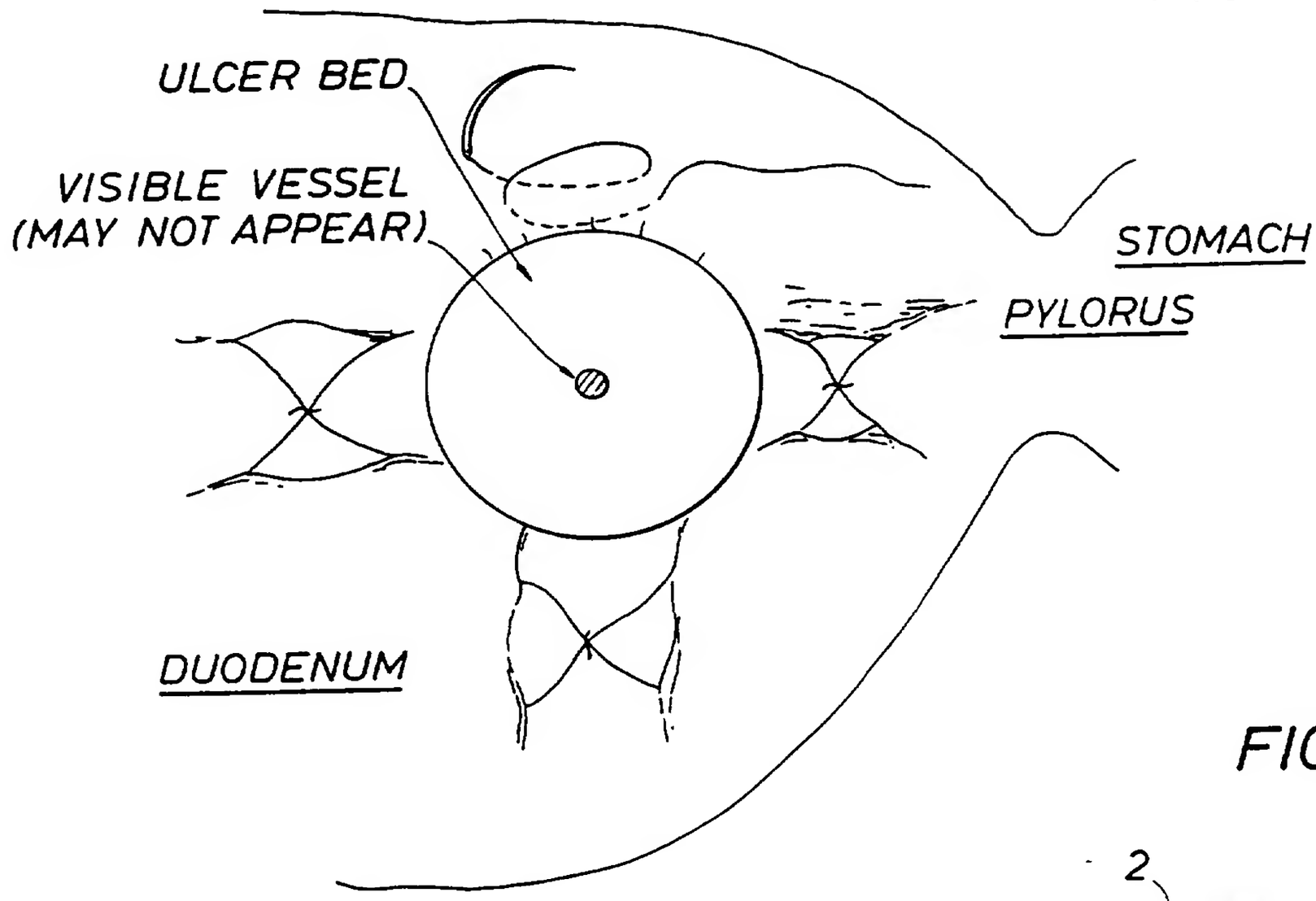


FIG. 2

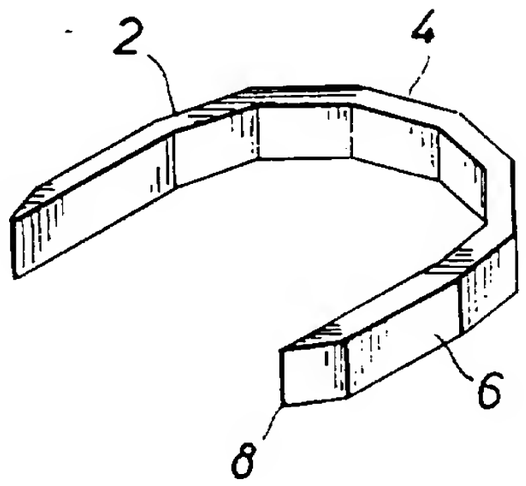


FIG. 3

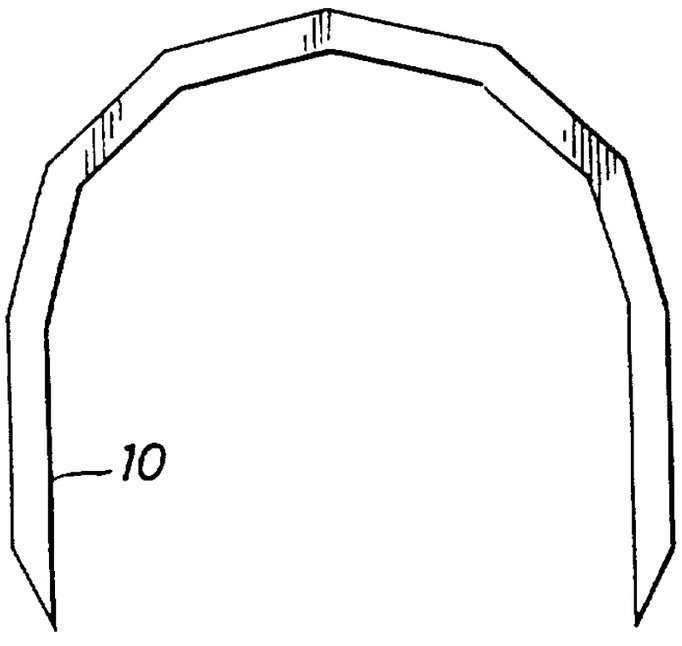


FIG. 4

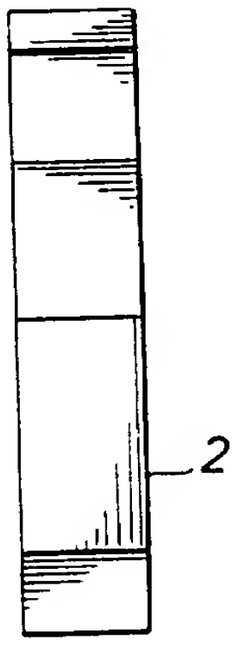


FIG. 5

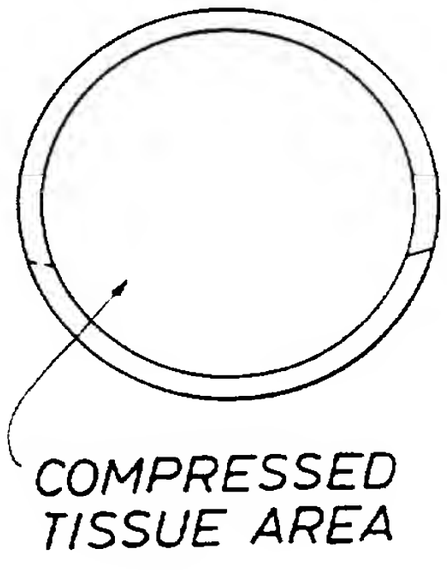


FIG. 6

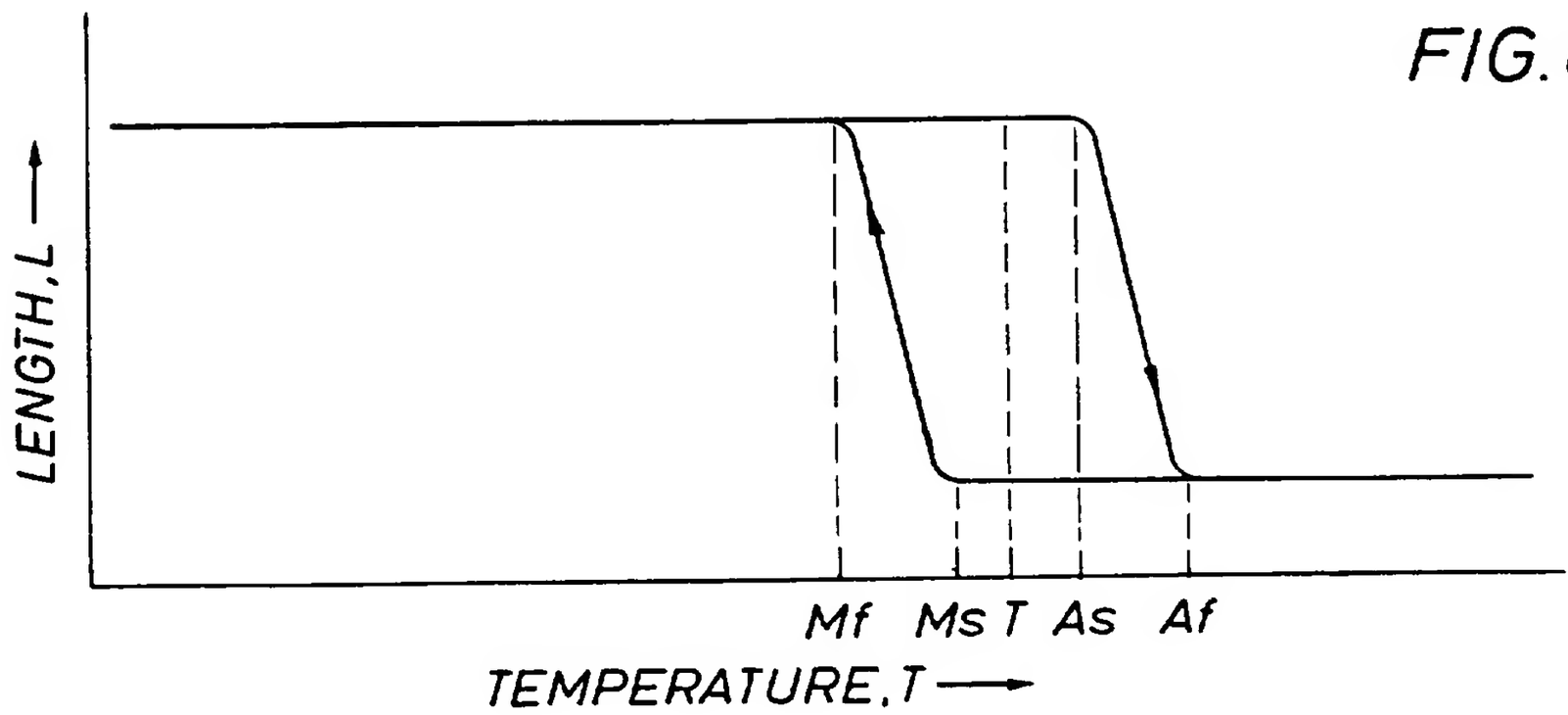


FIG. 7

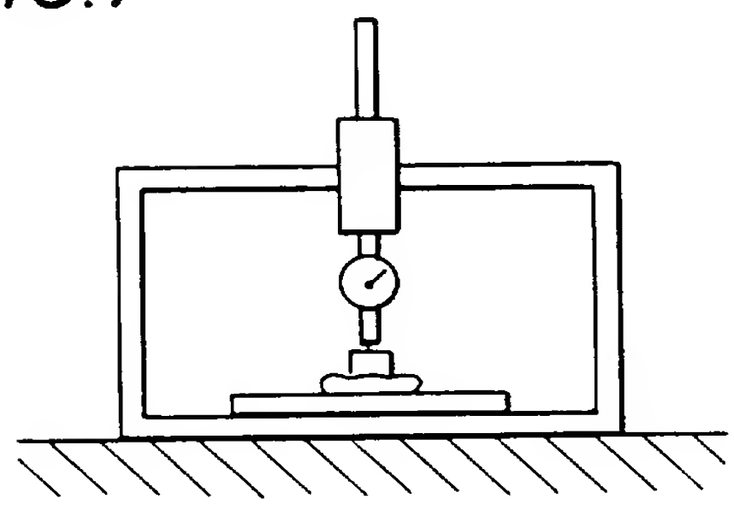
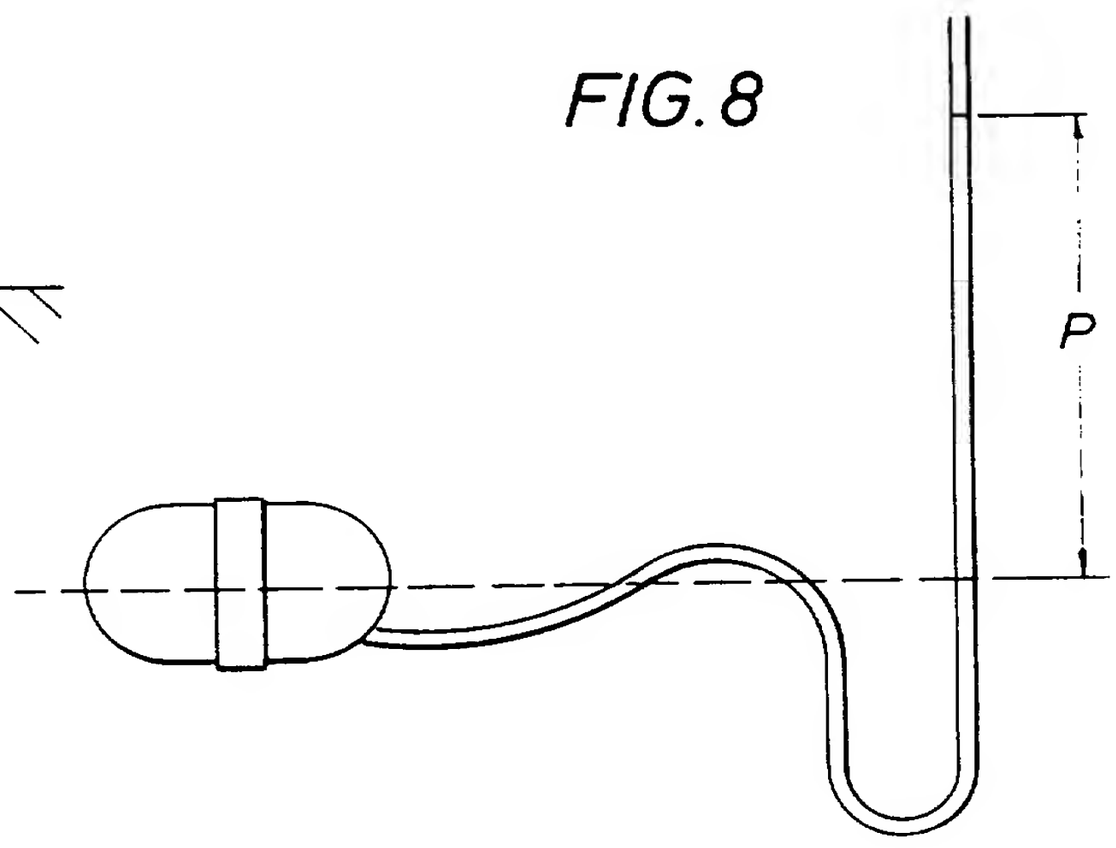


FIG. 8



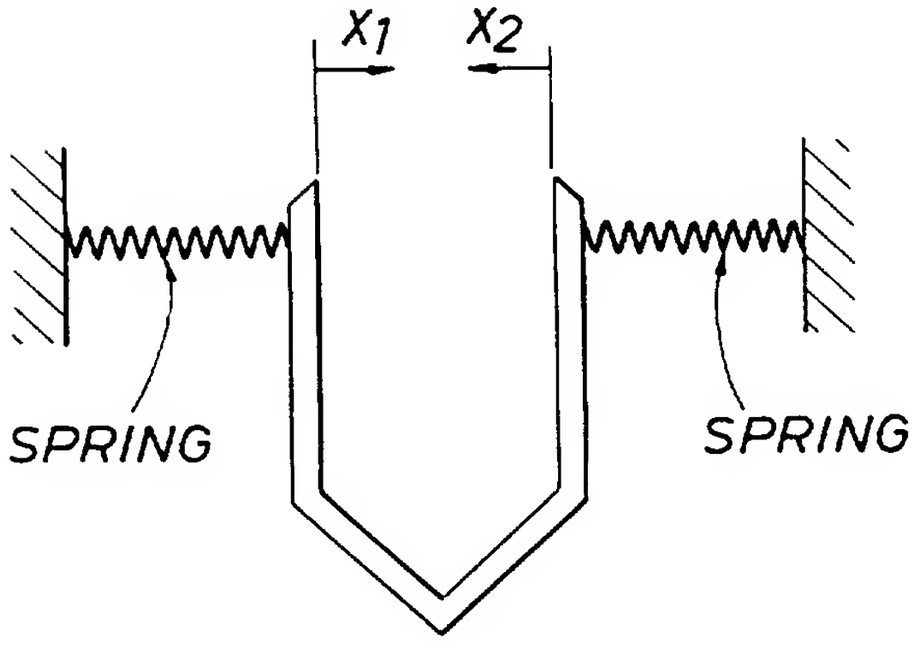


FIG. 9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US95/15397

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 17/04
US CL :606/78, 142, 219

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/78, 142, 219

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS

Search Terms: shape memory alloy; sma; NITINOL; nickel-titanium;

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 4,170,990 (BAUMGART ET AL.) 16 October 1979, see columns 1 and 2.	13, 14
A	US, A, 5,067,957 (JERVIS) 26 November 1991, see columns 2 and 3.	1-19
Y	US, A, 4,485,816 (KRUMME) 04 December 1984, col. 5, lines 6-29	1-10, 15-19

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search
09 APRIL 1996

Date of mailing of the international search report
01 MAY 1996

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